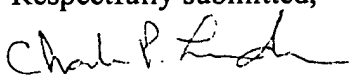
have been clarified by further defining the classes of chemotherapeutics that may be used in combination thiazolidinedione therapy.

G. Conclusion

Applicants believe that the present document is a full and complete response to the referenced Official Action. In conclusion, Applicants submit that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable Action is respectfully requested. Should the Examiner have any further questions or comments, or believe that certain clarifications might more readily progress the present application to issuance, a telephone call to the undersigned Applicants' representative at (512) 536-5674 is earnestly solicited.

Respectfully submitted,



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Date: August 29, 2002

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APPENDIX A: VERSION OF CLAIM AMENDMENTS MARKED TO SHOW CHANGES

1. (Twice amended) A method for inhibiting the growth of a cancer cell comprising

(i) contacting the cancer cell with a thiazolidinedione compound; and

(ii) contacting the cancer cell with a chemotherapeutic drug or irradiating the cancer cell with X-ray irradiation, UV-irradiation, γ-irradiation, or microwaves, in amounts effective to inhibit the growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

17. (Canceled) The method of claim 16, wherein the chemotherapeutic drug comprises an alkylating agent, mitotic inhibitor, antibiotic, nitrosurea, antimetabolite, corticosteroid hormone, or other antineoplastic agent.

18. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an alkylating [alklyating] agent.

19. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a mitotic inhibitor.

20. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an antibiotic.

21. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a nitrosourea.

22. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an antimetabolite.

23. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a corticosteroid hormone.

24. (Canceled) The method of claim 17, wherein the chemotherapeutic drug comprises an antineoplastic agent.

26. (Amended) The method of claim 16[17], wherein the thiazolidinedione and the chemotherapeutic drug are suitably dispersed in a pharmacologically acceptable formulation.

32. (Canceled) The method of claim 25, further comprising contacting the cancer cell with a therapeutic polynucleotide selected from the group consisting of a Dp gene, p21, p16, p27, E2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X_S and E1A; wherein the therapeutic polynucleotide is expressed in the cancer cell.

33. (Twice amended) A method for treating cancer in a patient comprising administering to the patient troglitazone and a chemotherapeutic drug in an amount effective to produce a therapeutic benefit; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

35. (Amended) A method of treating cancer in a patient comprising administering to the patient a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

36. (Twice amended) A method for treating microscopic residual cancer comprising the steps of:

(i) identifying a patient having a resectable tumor;

(ii) resecting said tumor; and

(iii) contacting the tumor bed with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

37. (Twice amended)A method for treating a subject having a tumor comprising the steps of:

(i) surgically revealing said tumor; and

(ii) contacting said tumor with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

38. (Twice amended) A method for treating a subject having a tumor comprising the step of perfusing said tumor, over an extended period of time, with a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

41. (Amended) A method for inhibiting the growth of a cancer cell comprising:

(i) contacting the cancer cell with a composition comprising troglitazone; and

(ii) contacting the cancer cell with a chemotherapeutic agent or irradiating the cancer cell, in amounts effective to inhibit growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

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APPENDIX B: PENDING CLAIMS (UNOFFICIAL)

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1. A method for inhibiting the growth of a cancer cell comprising

   (i) contacting the cancer cell with a thiazolidinedione compound; and

   (ii) contacting the cancer cell with a chemotherapeutic drug or irradiating the cancer cell with X-ray irradiation, UV-irradiation, γ-irradiation, or microwaves, in amounts effective to inhibit the growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

2. The method of claim 1, wherein the thiazolidinedione compound is a troglitazone.

3. The method of claim 1, wherein the thiazolidinedione compound is a pioglitazone.

4. The method of claim 1, wherein the thiazolidinedione compound is a rosiglitazone.

5. The method of claim 1, wherein the cancer cell is a mammalian cancer cell.

6. The method of claim 5, wherein the cancer cell is a human cancer cell.

7. The method of claim 1, wherein the contacting occurs *in vitro*.

8. The method of claim 1, wherein the contacting occurs *in vivo*.

9. The method of claim 1, wherein the cancer cell is selected from a group consisting of a bladder, blood, bone, bone marrow, brain, breast, colon, esophagus, gastrointestine, head, kidney, liver, lung, nasopharynx, neck, ovary, prostate, skin, stomach, and uterus cell.

10. The method of claim 9, wherein the cancer cell expresses PPAR-γ.

11. The method of claim 9, wherein the cancer cell is a bone cancer cell.

12. The method of claim 11, wherein the bone cancer cell is an osteosarcoma cell.

13. The method of claim 11, wherein the cancer cell is a precursor to osteosarcoma.

14. The method of claim 9, wherein the cancer cell is an ovarian cancer cell.

15. The method of claim 9, wherein the cancer cell is a renal cancer cell.

16. The method of claim 1, wherein the cancer cell is contacted with a chemotherapeutic drug.

18. The method of claim 16, wherein the chemotherapeutic drug comprises an alkylating agent.

19. The method of claim 16, wherein the chemotherapeutic drug comprises a mitotic inhibitor.

20. The method of claim 16, wherein the chemotherapeutic drug comprises an antibiotic.

21. The method of claim 16, wherein the chemotherapeutic drug comprises a nitrosourea.

22. The method of claim 16, wherein the chemotherapeutic drug comprises an antimetabolite.

23. The method of claim 16, wherein the chemotherapeutic drug comprises a corticosteroid hormone.

25. The method of claim 1, wherein the thiazolidinedione compound is contacted with a cancer cell by administering the thiazolidinedione regionally, endoscopically, intravenously,

intralesionally, percutaneously, subcutaneously, intraperitoneally, intratracheally, intramuscularly, or by perfusion.

26. The method of claim 16, wherein the thiazolidinedione and the chemotherapeutic drug are suitably dispersed in a pharmacologically acceptable formulation.

27. The method of claim 1, wherein the thiazolidinedione compound is contacted with the cancer cell at the same time as contact with the chemotherapeutic agent.

28. The method of claim 1, wherein the cancer cell is a tumor cell in a tumor.

29. The method of claim 28, further comprising resecting the tumor.

30. The method of claim 28, wherein the cancer cell is irradiated with X-ray irradiation, UV-irradiation, -irradiation, or microwaves.

31. The method of claim 30, wherein the thiazolidinedione compound is contacted with the cancer cell at the same time as irradiation.

33. A method for treating cancer in a patient comprising administering to the patient troglitazone and a chemotherapeutic drug in an amount effective to produce a therapeutic benefit; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

34. A method for inhibiting the cell cycle progression of a mammalian cancer cell comprising contacting the cell with an amount of troglitazone effective to inhibit the cell cycle progression of the cell.

35. A method of treating cancer in a patient comprising administering to the patient a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the

chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

36. A method for treating microscopic residual cancer comprising the steps of:

(i) identifying a patient having a resectable tumor;

(ii) resecting said tumor; and

(iii) contacting the tumor bed with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

37. A method for treating a subject having a tumor comprising the steps of:

(i) surgically revealing said tumor; and

(ii) contacting said tumor with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

38. A method for treating a subject having a tumor comprising the step of perfusing said tumor, over an extended period of time, with a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

39. The method of claim 27, wherein the thiazolidinedione and the chemotherapeutic agent are combined in a therapeutic formulation.

40. A method for inhibiting the growth of a cancer cell comprising:

(i) contacting the cancer cell with a composition comprising troglitazone; and

(ii) contacting the cancer cell with a chemotherapeutic agent or irradiating the cancer cell, in amounts effective to inhibit growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

41. The method of claim 40, wherein the cancer cell is contacted with a chemotherapeutic agent.

42. The method of claim 41, wherein the composition comprises troglitazone and a chemotherapeutic agent.

43. The method of claim 40, wherein the cancer cell is a bone cancer cell.

44. The method of claim 43, wherein the bone cancer cell is an osteosarcoma cell.

45. The method of claim 40, wherein the cancer cell is an ovarian cancer cell.

46. The method of claim 40, wherein the cancer cell is a renal cancer cell.

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APPENDIX A: ~~VERSION OF CLAIM AMENDMENTS~~ MARKED TO SHOW CHANGES

1. (Twice amended) A method for inhibiting the growth of a cancer cell comprising

(i) contacting the cancer cell with a thiazolidinedione compound; and

(ii) contacting the cancer cell with a chemotherapeutic drug or irradiating the cancer cell with X-ray irradiation, UV-irradiation, γ-irradiation, or microwaves, in amounts effective to inhibit the growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

17. (Canceled) The method of claim 16, wherein the chemotherapeutic drug comprises an alkylating agent, mitotic inhibitor, antibiotic, nitrosurea, antimetabolite, corticosteroid hormone, or other antineoplastic agent.

18. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an alkylating [alklyating] agent.

19. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a mitotic inhibitor.

20. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an antibiotic.

21. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a nitrosourea.

22. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises an antimetabolite.

23. (Amended) The method of claim 16[17], wherein the chemotherapeutic drug comprises a corticosteroid hormone.

24. (Canceled) The method of claim 17, wherein the chemotherapeutic drug comprises an antineoplastic agent.

26. (Amended) The method of claim 16[17], wherein the thiazolidinedione and the chemotherapeutic drug are suitably dispersed in a pharmacologically acceptable formulation.

32. (Canceled) The method of claim 25, further comprising contacting the cancer cell with a therapeutic polynucleotide selected from the group consisting of a Dp gene, p21, p16, p27, E2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X-$_S$ and E1A; wherein the therapeutic polynucleotide is expressed in the cancer cell.

33. (Twice amended) A method for treating cancer in a patient comprising administering to the patient troglitazone and a chemotherapeutic drug in an amount effective to produce a therapeutic benefit; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

35. (Amended) A method of treating cancer in a patient comprising administering to the patient a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

36. (Twice amended) A method for treating microscopic residual cancer comprising the steps of:

(i) identifying a patient having a resectable tumor;

(ii) resecting said tumor; and

(iii) contacting the tumor bed with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

37. (Twice amended)A method for treating a subject having a tumor comprising the steps of:

(i) surgically revealing said tumor; and

(ii) contacting said tumor with a therapeutically effective amount of troglitazone and a chemotherapeutic drug;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

38. (Twice amended) A method for treating a subject having a tumor comprising the step of perfusing said tumor, over an extended period of time, with a therapeutically effective amount of troglitazone and a chemotherapeutic drug; wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

41. (Amended) A method for inhibiting the growth of a cancer cell comprising:

(i) contacting the cancer cell with a composition comprising troglitazone; and

(ii) contacting the cancer cell with a chemotherapeutic agent or irradiating the cancer cell, in amounts effective to inhibit growth of the cancer cell;

wherein, the chemotherapeutic drug is an alkylating agent, an antimetabolite, an antitumor antibiotic, a corticosteroid hormone, a mitotic inhibitor, a nitrosurea, or a tumor necrosis factor.

Fwd All Rejected Claims

APPENDIX B:

CLEAN COPY OF THE CLAIMS (UNOFFICIAL)

1. A method for inhibiting the growth of a cancer cell comprising
(i) contacting the cancer cell with a thiazolidinedione compound; and
(ii) contacting the cancer cell with a chemotherapeutic drug or irradiating the cancer cell with X-ray irradiation, UV-irradiation, γ-irradiation, or microwaves, in amounts effective to inhibit the growth of the cancer cell.

2. The method of claim 1, wherein the thiazolidinedione compound is a troglitazone.

3. The method of claim 1, wherein the thiazolidinedione compound is a pioglitazone.

4. The method of claim 1, wherein the thiazolidinedione compound is a rosiglitazone.

5. The method of claim 1, wherein the cancer cell is a mammalian cancer cell.

6. The method of claim 5, wherein the cancer cell is a human cancer cell.

7. The method of claim 1, wherein the contacting occurs *in vitro*.

8. The method of claim 1, wherein the contacting occurs *in vivo*.

9. The method of claim 1, wherein the cancer cell is selected from a group consisting of a bladder, blood, bone, bone marrow, brain, breast, colon, esophagus, gastrointestine, head, kidney, liver, lung, nasopharynx, neck, ovary, prostate, skin, stomach, and uterus cell.

10. The method of claim 9, wherein the cancer cell expresses PPAR-γ.

11. The method of claim 9, wherein the cancer cell is a bone cancer cell.

12. The method of claim 11, wherein the bone cancer cell is an osteosarcoma cell.

13. The method of claim 11, wherein the cancer cell is a precursor to osteosarcoma.

14. The method of claim 9, wherein the cancer cell is an ovarian cancer cell.

15. The method of claim 9, wherein the cancer cell is a renal cancer cell.

16. The method of claim 1, wherein the cancer cell is contacted with a chemotherapeutic drug.

17. The method of claim 16, wherein the chemotherapeutic drug comprises an alkylating agent, mitotic inhibitor, antibiotic, nitrosurea, antimetabolite, corticosteroid hormone, or other antineoplastic agent.

18. The method of claim 17, wherein the chemotherapeutic drug comprises an alklyating agent.

19. The method of claim 17, wherein the chemotherapeutic drug comprises a mitotic inhibitor.

20. The method of claim 17, wherein the chemotherapeutic drug comprises an antibiotic.

21. The method of claim 17, wherein the chemotherapeutic drug comprises a nitrosourea.

22. The method of claim 17, wherein the chemotherapeutic drug comprises an antimetabolite.

23. The method of claim 17, wherein the chemotherapeutic drug comprises a corticosteroid hormone.

24. The method of claim 17, wherein the chemotherapeutic drug comprises an antineoplastic agent.

25. The method of claim 1, wherein the thiazolidinedione compound is contacted with a cancer cell by administering the thiazolidinedione regionally, endoscopically, intravenously, intralesionally, percutaneously, subcutaneously, intraperitoneally, intratracheally, intramuscularly, or by perfusion.

26. The method of claim 17, wherein the thiazolidinedione and the chemotherapeutic drug are suitably dispersed in a pharmacologically acceptable formulation.

27. The method of claim 1, wherein the thiazolidinedione compound is contacted with the cancer cell at the same time as contact with the chemotherapeutic agent.

28. The method of claim 1, wherein the cancer cell is a tumor cell in a tumor.

29. The method of claim 28, further comprising resecting the tumor.

30. The method of claim 28, wherein the cancer cell is irradiated with X-ray irradiation, UV-irradiation, -irradiation, or microwaves.

31. The method of claim 30, wherein the thiazolidinedione compound is contacted with the cancer cell at the same time as irradiation.

32. The method of claim 25, further comprising contacting the cancer cell with a therapeutic polynucleotide selected from the group consisting of a Dp gene, p21, p16, p27, E2F, Rb, APC, DC, NF-1, NF-2, WT-1, MEN-I, MEN-II, BRCA1, VHL, FCC, MCC, *ras*, *myc*, *neu*, *raf*, *erb*, *src*, *fms*, *jun*, *trk*, *ret*, *gsp*, *hst*, *bcl*, *abl*, Bax, Bcl-X-$_S$ and E1A; wherein the therapeutic polynucleotide is expressed in the cancer cell.

33. A method for treating cancer in a patient comprising administering to the patient troglitazone and a chemotherapeutic drug in an amount effective to produce a therapeutic benefit.

34. A method for inhibiting the cell cycle progression of a mammalian cancer cell comprising contacting the cell with an amount of troglitazone effective to inhibit the cell cycle progression of the cell.

35. A method of treating cancer in a patient comprising administering to the patient a therapeutically effective amount of troglitazone and a chemotherapeutic drug.

36. A method for treating microscopic residual cancer comprising the steps of:
(i) identifying a patient having a resectable tumor;
(ii) resecting said tumor; and
(iii) contacting the tumor bed with a therapeutically effective amount of troglitazone and a chemotherapeutic drug.

37. A method for treating a subject having a tumor comprising the steps of:
(i) surgically revealing said tumor; and
(ii) contacting said tumor with a therapeutically effective amount of troglitazone and a chemotherapeutic drug.

38. A method for treating a subject having a tumor comprising the step of perfusing said tumor, over an extended period of time, with a therapeutically effective amount of troglitazone and a chemotherapeutic drug.

39. The method of claim 27, wherein the thiazolidinedione and the chemotherapeutic agent are combined in a therapeutic formulation.

40. A method for inhibiting the growth of a cancer cell comprising i) contacting the cancer cell with a composition comprising troglitazone and ii) contacting the cancer cell with a chemotherapeutic agent or irradiating the cancer cell, in amounts effective to inhibit growth of the cancer cell.

41. The method of claim 40, wherein the cancer cell is contacted with a chemotherapeutic agent.

42. The method of claim 41, wherein the composition comprises troglitazone and a chemotherapeutic agent.

43. The method of claim 40, wherein the cancer cell is a bone cancer cell.

44. The method of claim 43, wherein the bone cancer cell is an osteosarcoma cell.

45. The method of claim 40, wherein the cancer cell is an ovarian cancer cell.

46. The method of claim 40, wherein the cancer cell is a renal cancer cell.